A CLINICOPATHOLOGICAL STUDY OF PERFORATING DERMATOSES

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Chennai - Tamilnadu.

CERTIFICATE

This is to certify that this dissertation titled “A clinicopathological study of perforating dermatoses” submitted by **DR.S.PRATHIBA** to the TamilNadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree branch – XII A, is a bonafide research work carried out by her under direct supervision and guidance.

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CONTENTS

INTRODUCTION

Perforating dermatoses represents a heterogenous group of disorders characterized by transepithelial elimination of dermal structures.

Transepithelial elimination (TEE) is the process in which material from the dermis is extruded through the epidermis to the exterior with little or no disruption of the surrounding structures. The extruded material may include inflammatory cells, red cells, microorganisms and extracellular substances, such as mucin or altered connective tissue components.[1]

Perforating dermatoses can occur in various clinical settings.

1. As primary perforating dermatoses
2. Associated with systemic diseases
3. As a secondary component of primary dermatoses

1. Primary perforating dermatoses

a. Kyrle's disease (hyperkeratosis follicularis et parafollicularis in cutem penetrans)
b. Reactive perforating collagenosis (RPC)
c. Elastosis perforans serpiginosa(EPS)
d. Perforating folliculitis(PF).

2. Associated with systemic diseases

Acquired perforating dermatoses, initially, it was described in association with renal disease and /or diabetes mellitus. But in recent years, it has been reported in patients with malignant,[2,3] hepatic[4], endocrinological disorders,[4] AIDS,[5] tuberculosis,[6] pulmonary aspergillosis,[7] neurodermatitis,[4] atopic dermatitis[8] and scabies.[9]The clinical and histopathological findings may resemble any of these four primary perforating dermatoses (Kyrle's, RPC, EPS, PF).[10]

3. As a secondary component in primary dermatoses

Transepithelial elimination can occur as a secondary component of primary diseases such as granuloma annulare, pseudoxanthoma elasticum, chondrodermatitis nodularis helices, lichen nitidus, lichen planus, keratoacanthomas and necrobiosis lipoidica.

REVIEW OF LITERATURE

HISTORY [11]

1916 - Kyrle's disease was described by Kyrle as hyperkeratosis follicularis et parafollicularis in cutem penetrans.

1953 - Elastosis perforans serpiginosa(EPS) was described by Lutz as keratosis follicularis serpiginosa.

1955 - Meischer described the histologic findings, naming it Elastoma intrapapillare perforans verruciforme.

1967 - Reactive perforating collagenosis(RPC) was first reported in a child by Mehregan, Schwartz and Livingood.

1968 - Perforating folliculitis (PF) was included in the primary perforating dermatoses by Mehregan and Coskey.

1976 – Formerly known as pseudoxanthoma elasticum coexisting with elastosis perforans serpiginosa, periumbilical perforating pseudoxanthoma elasticum was redescribed later by Lund and Gilbert as a distinct entity.[12]

1979 – The term periumbilical perforating pseudoxanthoma elasticum was first proposed by Hicks et al.[13]

Later Neldner and Martinez-Hernandez proposed the term "Localized acquired cutaneous pseudoxanthoma elasticum", as they believed the process was "acquired" and was lacking "systemic involvement".[14]

EPIDEMIOLOGICAL ASPECTS OF PERFORATING DERMATOSES

Incidence

The perforating diseases are found worldwide. In patients receiving dialysis, acquired perforating dermatosis is rather common, with a prevalence of about 11%.[15]

Race

Perforating calcific elastosis (Periumbilical perforating pseudoxanthoma elasticum) is common in black women.[16]

Familial form

Childhood form of reactive perforating collagenosis is often familial.[17]

Childhood elastosis perforans serpiginosa is occasionally familial.[18]

Inheritance pattern

Reactive perforating collagenosis – Both autosomal dominant and autosomal recessive.[19]

Elastosis perforans serpiginosa - Autosomal dominant.[20]

Kyrle's disease – Autosomal recessive.[21]

Age

Inherited type – childhood or early adulthood.

Acquired type – middle aged adults.

Sex

Elastosis perforans serpiginosa mainly affects nearly four times more men than women.

But in reactive perforating collagenosis and acquired perforating dermatoses the sex distribution is equal.

Perforating folliculitis is said to be more common in women.[11]

In Kyrle's disease, a female preponderance is noted in some series.[2]

Perforating periumbilical calcific elastosis is seen predominantly in women.[16]

Seasonal variation

Recurrences in winter and cold exacerbation is present in familial reactive perforating collagenosis.[23] One study reported frequent recurrences in summer than in winter owing to longer duration of the former in a case of familial reactive perforating collagenosis.[24]

ETIOPATHOGENESIS OF PERFORATING DERMATOSES

The precise etiopathogenesis for the perforating disorder is unknown.

Epithelium becomes hyperplastic and eventually surrounds the abnormal connective tissue, just as it appears to do with wood splinters or other foreign bodies.

Primarily perforating diseases may be due to either genetic or acquired abnormalities of collagen or elastic fibers.

Fibronectin levels have been shown to be increased in the serum of patients with diabetes mellitus and uremia, and it has also been found to be increased in the skin at sites of perforating lesions.[25]This may be significant, since fibronectin plays a role in epithelial cell signaling, locomotion and differentiation. It binds to type IV collagen (the type found in basement membrane) and to keratinocytes, and may incite epithelial proliferation and perforation.

Increased expression of TGF-β3 has also been observed in the epidermis and dermis near the sites of perforation in reactive perforating collagenosis, but this enhanced expression occurs in general wound healing reactions as well.[26]

Other proposed pathomechanisms include abnormal vitamin A metabolism,[27] enzyme release from neutrophils,[28] microangiopathy related diabetes, salt water chemical burns[29] and an imbalance in the expression of

metalloproteinases and their tissue inhibitors. The metalloproteinases is assumed to influence the transepithelial channel formation by loosening the interkeratinocyte bonds, disrupting the basement membrane, and detaching the collagen fibers. This is supported by increased levels of metalloproteinases after epidermal injury (ex.scratching) after hypoxic condition or in diabetes state.[9] Deposition of substances such as uric acid, hydroxyapatite, silicon[30] or other materials[31] has also been implicated in the pathogenesis of perforating disorders.

Trauma is a major trigger of perforating disorders, although the molecular basis to explain the development of lesions after trauma is unclear. Many patients exhibit the Koebner phenomenon, and lesions can be produced experimentally by traumatizing the skin[32] and after laser hair removal.[33]

Kyrle's disease

The exact etiopathogenesis of this disease is not well understood, but a genetic role has been suggested in some cases. Familial cases may occur.[34] Many cases occur in association with diabetes mellitus,[35,36] chronic renal failure[37] and liver disease.[38]

The primary event is claimed to be a disturbance of epidermal keratinization characterized by the formation of dyskeratotic foci and acceleration of the process of keratinization. This leads to the formation of keratotic plugs with areas of parakeratosis. Because the rapid rate of

differentiation and keratinization exceeds the rate of cell proliferation, the parakeratotic column gradually extends deeper into the abnormal epidermis leading to the perforation of the parakeratotic column into the dermis. The keratotic plug acts as a foreign body, penetrate the epidermis and incite a granulomatous inflammatory reaction.[39]

Reactive perforating collagenosis

The cause is unknown but the condition is often familial.[17,40] It is usually precipitated by environmental cold[17] or trauma. It has been typically associated with diabetes and hemodialysis, also reported with hypothyroidism and hyperthyroidism, liver disorders, hodgkin's lymphoma,[2] treacher-collins syndrome,[41] herpes zoster[42,43] and periampullary carcinoma.[44]

An abnormal response to superficial trauma such as scratching may be implicated in the acquired form. This leads to focal damage to collagen, which then extruded as a result of necrolysis of the overlying epidermis.[45] There is transepidermal elimination of histochemically altered collagen only, as the collagen fibrils appear intact with regular periodicity by electron microscopy.[46]

Elastosis perforans serpiginosa

The cause of elastosis perforans serpiginosa is not known, but a genetically determined defect of elastic tissue may be involved in the idiopathic type.[18] In some 40% of cases, there is an associated systemic condition or

connective tissue disorder, such as Down's syndrome,[47,48] osteogenesis imperfecta,[49] cutis laxa,[50] Ehler's Danlos syndrome, Marfan's syndrome, acrogeria,[51] scleroderma,[52] Pseudoxanthoma elasticum, Rothmund Thomson syndrome,[53] diabetes[54] and renal failure.[55] Similar cutaneous lesions have been reported in patients with Wilson's disease and cystinuria receiving long term penicillamine therapy.[50,56,57]

The thickened elastic fibers act as mechanical irritants or "foreign bodies" and provoke an epidermal response in the form of hyperplasia. The epidermis then envelops the irritating material and eliminates it through transepidermal channels. The degeneration of the elastic fibers within the channels probably is caused by proteolytic enzymes set free by degenerating inflammatory cells.[53]The channel is formed as a reactive phenomenon through which the foreign bodies are extruded.

In patients on penicillamine therapy, a local copper depletion or a direct effect of penicillamine on elastin synthesis – disruption of desmosine cross links within elastin may be responsible for the formation of the abnormal elastic fibers which are then eliminated transepidermally.[56,58]

Elastic tissue damage appears to occur in other organs as well, a feature generally lacking in the usual idiopathic form of the disease.[58,59] The nature of the defect in the idiopathic form is unknown, but it is possible that perforating elastosis is the final common pathway for more than one abnormality of elastic

fibers.[60,10] This theory is compatible with the recent finding of an elastin receptor in keratinocytes immediately surrounding the elastic materials being eliminated in lesions of elastosis perforans serpiginosa. The elastin receptor may be involved in the interaction between keratinocytes and elastin.[61]

Perforating folliculitis

The etiology of perforating folliculitis is unknown, although minor mechanical trauma may play a role. It can occur as an isolated finding unrelated to other disease states and also be associated with renal failure often with hemodialysis,[62] psoriasis,[63] juvenile acanthosis nigicans, human immunodeficiency virus (HIV) infection[64] and primary sclerosing cholangitis.[65]

Perforating folliculitis is the end result of abnormal follicular keratinization that most likely is caused by chemical or physical irritation and even chronic rubbing. A portion of a curled up hair is often seen close to or within the area of perforation or even in the dermis, surrounded by a foreign body granuloma.[39] Mehregan first proposed that curled hairs within follicular canals may act as springs penetrating the lateral follicular wall, thereby initiating the process of transepithelial elimination.[66] Support for this concept has been provided by an ultrastructural study of acquired perforating dermatoses that showed hair fragments within transepidermal channels, even in patients in whom follicular involvement was not demonstrable on routine light microscopy. Factors that may promote coiling of hair include follicular hyperkeratosis

(occasional perforated follicles can be identified in keratosis pilaris) or contact dermatitis (ex.resulting from formaldehyde in clothing).

Acquired perforating dermatoses

Several theories have been proposed for the pathogenesis of acquired perforating dermatoses. Microtrauma due to pruritus and scratching,[67] diabetes mellitus related microangiopathy,[68] epidermal or dermal change related to metabolic derangements[69,70] and deposition of substances that cannot be removed with dialysis[62] are the most commonly proposed theories.

Perforating calcific elastosis

The etiologic nature of perforating calcific elastosis has been debated. Some hypothesize that it is an acquired lesion developing as a consequence of local cutaneous trauma from such factors as obesity, multiple pregnancies, ascites, or multiple abdominal surgeries.[13,14,71] It has been suggested that the stretching of the skin due to repeated pregnancies, obesity and abdominal surgeries promote elastic fibres degeneration resulting in perforating calcific elastosis.[72] Association with chronic renal failure has been noted with apparent regression of skin lesions after hemodialysis.[73]

Others have argued that perforating calcific elastosis may represent a localized cutaneous expression of hereditary pseudoxanthoma elasticum.[74]The

disorder may represent a spectrum ranging from a purely acquired form with no systemic manifestation to an inherited form with limited systemic expression.

CLINICAL FEATURES

Kyrle's disease

Kyrle's disease, as traditionally described, consists of hyperkeratotic papules 2 to 8 mm in diameter containing a central cone shaped plug.[75,76] They are multiple, discrete or confluent and they may coalesce to form a verrucous plaque,[77] large irregular or circinate lesions.[38] The papules may be follicular or extrafollicular in location and brownish black in colour. There is a predilection for the lower extremities but lesions may also occur on the upper limbs and less often on the head and neck.[76,78] Palmar and plantar surfaces are rarely involved.[79] Lesions have even been described on the conjunctiva and buccal mucosa.[80] Koebner phenomenon may occur, especially in the cubital and popliteal fossae. Onset is usually in the fourth decade.

Reactive perforating collagenosis

The inherited form starts in infancy and early childhood. After superficial trauma, patient develop pin head sized skin coloured papules that grow to a diameter of about 6 mm over the following 3 to 5 weeks and then develop a central area of umbilication in which keratinous material is lodged. The discrete papules may be numerous and involve sites of frequent trauma such as backs of

hands, forearms, elbows and knees.[45] The sole of the foot is a rare site.[81] The lesions regress spontaneously in 6 to 8 weeks to leave a hypopigmented area or slight scar usually varioliform in nature. New lesions develop as older lesions are involuting and this may continue into adult life.[82]

There is often a history of superficial trauma; such as a scratch or insect bite.[45,83] Lesions have been induced experimentally by trauma.[32] The papules can also be provoked by inflamed acne lesions; but deep incisions do not produce these lesions.

The acquired form occurs in adults with history of diabetes mellitus and renal failure and may be associated with intense pruritus.

Elastosis perforans serpiginosa

Elastosis perforans serpiginosa is a rare disorder beginning during childhood or early adulthood i.e 6 to 20 years.

Skin lesions consist of hyperkeratotic or umbilicated papules ranging from 2mm to 5 mm characteristically arranged in a linear, serpiginous or circinate pattern. Skin within these serpiginous arcs is often atrophic. The individual papules may remain small or may enlarge slightly to assume a crateriform appearance with an elevated edge and a central plug. The annular rings may reach a diameter of 15 to 20 cm but are usually smaller. Most patients experience no symptoms or only mild pruritus.[53,84]

The most common site of involvement are back and sides of neck, but the lesions may also occur on the cheeks, arms or thighs and trunk and are sometimes generally symmetrical. Rarely, the lesions are generalized.[85,86] They may persist for several years but eventually involute spontaneously to leave reticulate atrophic scars. Biopsy scars readily become keloidal.

In rare instances, elastic tissue in the endocardium, bronchiolar walls, and arteries is involved. Rupture of the aorta has been reported.[59]

Perforating folliculitis

Perforating folliculitis is a perforating disorder that has many features overlapping with Kyrle's disease. This relatively uncommon disorder is usually observed in the second to fourth decades of life.

It is manifested by discrete, 2 – 8 mm diameter scaly keratotic folliculocentric papules with small central keratotic plugs and varying degrees of erythema. Compression of papules may yield keratin debris and a coiled hair or hair fragments. There is a predilection for the extensor surfaces of the extremities and the buttocks.[60] It may persists for months or years; although periods of remission often occur.

Often lesions are asymptomatic, although pruritus may be a striking feature, especially in patients with renal insufficiency. The Koebner

phenomenon usually is not readily demonstrable, but a linear configuration occasionally can be observed.

A case of progressive generalized perforating folliculitis has been reported to be associated with erythroderma, keratoderma of the palms and soles, alopecia of the scalp and eyebrows, and nail changes. Accompanying jaundice has been observed in patients with underlying liver disease.[87]

Acquired perforating dermatosis

Acquired perforating dermatosis has been used as a catch all term for those examples of perforating disease arising in adults, usually in association with diabetes mellitus and or the pruritus of renal failure.

Clinically, the lesions range from hyperkeratotic papules and nodules containing a central cone shaped plug resembling kyrle's disease to reactive perforating collagenosis – like hyperkeratotic, plugged, umbilicated papules, nodules and plaques to erythematous, follicular infiltrating papules and nodules mimicking perforating folliculitis. Annular plaques and erythematous pustules have also been described, with histologic features of reactive perforating collagenosis and perforating folliculitis, respectively.

Extensor surfaces of the lower extremities were the most commonly involved site, followed by the upper extremities, trunk and head. The lesions are

frequently pruritic and scratching can lead to a koebner phenomenon with linear umbilicated papules arising in excoriated skin.[88]

Perforating calcific elastosis

The onset of the disease is in the fifth to sixth decade of life in perimenopausal women.[89]These localized lesions usually occur in the periumbilical area in obese, multiparous black women[16] and rarely over the breast.[90] Most reported cases have been hypertensive.[73]

Initial eruption may contain asymptomatic or mildly pruritic erythematous papules, plaques or nodules. Over the course of several months or years, the lesions tend to resolve, leaving a well demarcated, hyperpigmented, reticulate, atrophic central plaque with raised, scaly border. Discrete, horny, hyperkeratotic papules may be scattered around the periphery. Lesions range in size from 2 – 15 cm and may be circular or oval.[90]

None of the systemic features of pseudoxanthoma elasticum occurs in perforating calcific elastosis.

HISTOPATHOLOGY

In all the perforating diseases, transepithelial elimination is the final common pathway whereby the altered dermal substances are extruded. There is a plug of crusting or hyperkeratosis, with variable parakeratosis, depending upon the stage of the lesion.

Sections from multiple levels through the tissue may need to be examined to find the site of perforation. Early lesions of even typical perforating dermatoses may not show typical features. Early stage showed exocytosis of inflammatory cells and alteration of elastic fibers in dermis, while evidence of perforation in basement membrane was evident only in older lesions.[91]

The special stains such as Verhoeff Van Gieson (VVG) and Masson Trichrome stains are most helpful. In VVG stain, collagen fibers appear red and elastic fibers black. In Masson Trichrome collagen fibers are stained blue or green.

Kyrle's disease[92,93]

The essential histopathologic findings include,

1. A follicular or extrafollicular cornified plug with focal parakeratosis embedded in an epidermal invagination.
2. Basophilic cellular debris in the plug which does not stain for collagen and elastic fibers.
3. Abnormal vacuolated and /or dyskeratotic cells extending to the basal cell layer.
4. Irregular epithelial hyperplasia.
5. A pronounced granulomatous reaction composed of inflammatory cells such as lymphocytes, occasional neutrophils and sometimes a few foreign

body giant cells seen when the keratotic plug is in contact with the dermis.

Follicular involvement present, particularly in those with chronic renal failure where overlap with perforating folliculitis occurs. Eccrine duct involvement was present in one atypical case reported in the literature.[79]

Reactive perforating collagenosis[45,67,94]

The appearances vary with the stage of evolution of the lesion. In early lesions, there is acanthosis of the epidermis and an accumulation of basophilic collagen in the dermal papillae.

In established lesions, there is a vertically oriented, shallow cup shaped invagination of the epidermis, forming a short channel filled with a plug consisting of parakeratotic keratin, basophilically altered collagen bundles and inflammatory debris. The channel is lined by acanthotic epithelium along the sides. The underlying epidermis is thin with fine slits through which basophilic collagen fibers in vertical orientation are extruded. Sometimes there is a complete break in the epidermis.[95] Nuclear material derived from neutrophils, and neutrophils themselves, are present in the extruded material.[6,96]

Masson trichrome stain must be done to confirm that the fibers are collagen.

Elastosis perforans serpiginosa[53,60,94,97]

The earliest change is the development of elastotic staining tissue and basophilic debris in the dermis that is engulfed by the overlying epidermis.

In fully developed lesions, there is a localized area of hyperplastic epidermis, associated with a narrow channel that may be straight, wavy or of corkscrew shape through which the basophilic nuclear debris and brightly eosinophilic thick coarse fragmented elastic fibers are being eliminated. A keratinous plug usually overlies this channel, which may take the form of a dilated infundibular structure or a more oblique canal coursing through the hyperplastic epidermis, follicular epithelium or the acrosyringium. An inflammatory cell infiltrate accompanies the fibers in the channel.

Abnormal elastic fibers are seen in the upper dermis in the vicinity of the channel. In this zone, the elastic fibers are increased in size and number. As these fibers enter the lower portion of the channel, they maintain their normal staining characteristics, but as they approach the epidermal surface, they may not stain as expected with elastic stains and become brightly eosinophilic. They will stain with the Giemsa method.

A few foreign body giant cells and inflammatory cells are often present in the dermis adjacent to the channel. In older lesions, there is focal dermal

scarring and usually an absence of elastic fibers. Verhoeff van Gieson stain is used for elastic fibers which stains it black in colour.

In penicillamine related cases, there is an increased number of thickened elastic fibers in the reticular dermis and less hyperplasia of elastic fibers in the papillary dermis, except in the areas of active transepidermal elimination.[98] The elastic fibers are irregular in outline with buds and serrations. This may be discerned in haematoxylin and eosin stained preparations, but it is well shown by elastic tissue stains[99] or in Epon – embedded thin sections stained with toluidine blue.[58]

Perforating folliculitis[100,60]

The main pathologic abnormalities consist of:

1. A dilated follicular infundibulum filled with compact ortho and parakeratotic cornified cells.

2. Degenerated basophilic staining material, comprised of granular nuclear debris from nuclear neutrophils, other inflammatory cells, and degenerated collagen bundles.

3. The follicular epithelium is disrupted in one or more areas in the infundibulum.

4. The adjacent dermis shows degenerative changes involving the connective tissue, and sometimes the altered collagen and refractile eosinophilically altered elastic fibers are seen entering the perforation.

5. A variable perifollicular inflammatory cell infiltrate composed of lymphocytes, histiocytes; and neutophils is present in the dermis.

6. A curled hair shaft is sometimes present.

Acquired perforating dermatosis

Biopsy findings in acquired perforating dermatosis vary according to the stage of evolution of the lesion. They may resemble any one of the primary perforating disorders. In other cases it may be less specific, with amorphous degenerated material within the perforations. This material often cannot be clearly identified as collagen or elastic fibers, but sometimes both are present.[10]

Epidermal invagination filled with keratotic plug admixed with cellular debris and neutrophils in the absence of follicular involvement, without demonstrable collagen or elastin is reminiscent of Kyrle's disease. When vertically oriented collagen, Masson trichrome positive collagen bundles are present within a perforation, the findings are suggestive of reactive perforating collagenosis. When perforation is associated with a follicle, the findings resemble perforating folliculitis. Perforation associated with elastic Van Gieson

positive elastic fibers within a transepidermal channel, as seen in elastosis perforans serpiginosa, has also been described.[55,88]

Patterson et al[63] reported a patient who had multiple lesions biopsied, which variably showed histologic features of reactive perforating collagenosis, perforating folliculitis, and Kyrle's disease. Moreover, Rapini and coworkers[10] reported combined transepidermal elimination of both collagen and elastin in their four patients with acquired perforating dermatosis.

Perforating calcific elastosis

Histological examination reveals numerous altered basophilic elastic fibres in the reticular dermis. They are short, thick, frayed, curled and are encrusted with calcium salts. Von Kossa stain is used to stain calcium.[39] Channels extruding inflammatory and elastotic debris from the reticular dermis to the overlying epidermis is seen. Eosinophilic intrapapillary elastoma may also be observed.[72]

AIM OF THE STUDY

1. To find out the incidence of perforating dermatoses among patients attending the skin OPD.

2. To delineate the clinical and histopathological features of various types of perforating dermatoses.

3. To find out the potential relationship existing between the perforating dermatoses and systemic disease.

MATERIALS AND METHODS

The material for this study was from the patients attending the skin OPD, Government Rajaji Hospital, Madurai Medical College, Madurai during the period from June 2008 to June 2010.

Inclusion criteria

All patients diagnosed clinically as perforating dermatoses and supported by histopathological examination.

Exclusion criteria

1. Patients who were unwilling for the study.

A detailed history was elicited with particular reference to age of onset, duration, site, morphology of lesions, progression, presence or absence of itching, systemic symptoms, occupation and family history. Detailed history of diabetes, renal failure, liver disease, endocrinological disorder and internal malignancy were also recorded.

A thorough general examination, systemic examination and dermatological examination were done. Digital photographs were taken.

Detailed examination of skin lesion which includes morphology of skin lesions, distribution of lesions, number of lesions, pigmentary changes and scarring were all recorded.

Laboratory investigations like blood sugar, urea, serum creatinine, liver function tests, urine examination, serology for human immunodeficiency virus (HIV), hepatitis (HBV, HCV) and complete hemogram were done. Special investigations like thyroid profile, serum calcium and ultrasonogram were performed wherever necessary.

Skin biopsies were done after getting informed consent. After thorough cleaning of the selected part with spirit or povidone iodine solution, the area was infiltrated with 2% lignocaine and a bit of the lesional skin was removed by punch biopsy. The specimens were preserved in 10% formalin and submitted for histopathological examination to the department of Pathology, Madurai Medical College. Specimens were studied with routine haematoxylin & eosin stain and special stains like Verhoeff van Gieson, Masson trichrome and Von Kossa wherever necessary.

A descriptive analysis of the clinical features, laboratory parameters and histopathological features of various perforating dermatoses was done. The data was analyzed and compared with published literature.

OBSERVATIONS AND RESULTS

Thirty five patients with clinical features of perforating dermatoses were seen during the study period from June 2008 to June 2010. Out of these, 5 patients were excluded from the study as they were not willing for the skin biopsy.

Thirty patients with clinical and histopathological features of perforating dermatoses were included in the study. The following observations were made.

Table 1: Types of perforating dermatoses

Types of perforating dermatoses	No. of patients	Percentage (%)
Kyrle's disease	16	54%
Reactive perforating collagenosis	13	43%
Perforating calcific elastosis	1	3%
Total	30	100%

Kyrle's disease was the commonest type (54%) followed by reactive perforating collagenosis (43%) and perforating calcific elastosis (3%).

Table 2:

Types of perforating dermatoses	Inherited	Acquired
Kyrle's disease	-	16
Reactive perforating collagenosis	9	4
Perforating calcific elastosis	-	1
Total	9	21

Among the perforating dermatoses, acquired form (70%) was more common than inherited form (30%).

AGE DISTRIBUTION

The age of onset in the acquired group was

Table 3:

Age of onset	KD	RPC	PCE	Total	Percentage
0 – 10	-	-	-	-	-
11 – 20	-	-	-	-	-
21 – 30	1	-	-	1	5
31 – 40	2	2	-	4	19
41 – 50	5	-	1	6	29
51 – 60	6	1	-	7	33
61 – 70	2	1	-	3	14
Total	16	4	1	21	100

KD - Kyrle's disease

RPC –Reactive perforating collagenosis

PCE – Perforating calcific elastosis

The age of onset of majority of the patients (62%) in the acquired group was between 41 – 60 years.

The age of onset in the inherited group was

Table 4:

Age of onset	RPC	Percentage (%)
0 – 10	2	22
11 – 20	7	78
Total	9	100

RPC –Reactive perforating collagenosis

The age of onset of majority of the patients (78%) in the inherited group was between 11 – 20 years.

Table 5: Age at presentation

Age at presentation	Inherited	Acquired
0 – 10	-	-
11 – 20	1	-
21 – 30	2	1
31 – 40	4	4
41 – 50	-	6
51 – 60	2	7
61 – 70	-	3
Total	9	21

According to our study, in the inherited group, 67% of the patients were between 21 – 40 years of age when they presented to us.

In the acquired form, the age at presentation of majority of the patients (62%) were between 41 – 60 years.

SEX DISTRIBUTION

20 patients were males and 10 patients were females.

Table 6: Sex distribution

Types of perforating dermatoses	Male	Female
Kyrle's disease	11	5
Reactive perforating collagenosis	9	4
Perforating calcific elastosis	-	1
Total	20	10

FAMILY HISTORY

Family history of perforating dermatoses was present in all the 9 cases (100%) in the inherited group.

SEASONAL VARIATION

Cold exacerbation was seen in 5 patients (56%) with familial reactive perforating collagenosis.

DURATION

The mean duration of disease was 7 years, with a maximum of 46 years and a minimum of 1 month.

MORPHOLOGY

Different types of lesions were observed. In 16 (53%) of the patients, the lesions were hyperkeratotic papules and in 13 (43%) hyperkeratotic, plugged, umbilicated papules and plaques were apparent. Erythematous papules arranged in annular and serpiginous pattern in the periphery of the central atrophic plaques were noted in 1 patient (3%).

DISTRIBUTION

Table 7: Site of involvement

Region	No. of patients	Percentage (%)
Head	5	23
Trunk	17	57
Upper extremities	19	63
Lower extremities	22	73

Lower extremities (73%) were the most commonly involved site, followed by the upper extremities (63%), trunk (57%) and head (23%).

SYMPTOMS

The presenting symptoms of the patients were itching in 63% and pain in 7%. 30% of patients were asymptomatic.

Table 8: Symptoms

Symptoms	No: of patients	Percentage (%)
Itching	19	63%
Pain	2	7%
Asymptomatic	9	30%
Total	30	100%

KOEBNER PHENOMENON

Koebner phenomenon was seen in 16 (53%) patients.

Table 9:

Types of perforating dermatoses	Total no. of patients	No. of patients with koebner phenomenon
KD	16	10
RPC	13	6
PCE	1	-
Total	30	16

KD - Kyrle's disease

RPC –Reactive perforating collagenosis

PCE – Perforating calcific elastosis

HISTOPATHOLOGY

Table 10: Biopsy findings

Biopsy findings	**KD**	**RPC**	**PCE**
Parakeratosis	12	8	-
Hyperkeratosis	16	10	1
Keratotic plugging	15	9	1
Acanthosis	16	11	1
Dyskeratotic cells	5	-	-
Transepidermal channel			
Keratin	16	9	1
Cellular debris	13	7	1
Altered collagen fibers	-	13	-
Altered elastic fibers	-	-	1
Papillary dermis			
Lymphocytes	10	4	1
Neutrophils	12	6	1
Altered collagen fibers	-	13	-
Altered elastic fibers	-	-	-
Reticular dermis			
Altered elastic fibers	-	-	1

KD - Kyrle's disease

RPC –Reactive perforating collagenosis

PCE – Perforating calcific elastosis

Histopathological evaluations revealed three types of lesions.

1. Histopathological features of 16 (54%) cases showed epidermal invagination filled with keratotic plug admixed with cellular debris and neutrophils. In biopsy specimens of these 16 patients, Masson trichrome and elastic van Gieson stains were negative in the epidermis and in the crater. Hence, the overall histological appearance in these 16 cases was consistent with Kyrle's disease.
2. Histopathological features of 13 (43%) cases showed cup shaped invagination of the epidermis filled with a plug consisting of keratin, cellular debris and neutrophils. There were vertically oriented collagen bundles at the base of the lesions in five of these thirteen cases. Masson trichrome staining showed transepidermal elimination of collagen in all these thirteen cases. Elastic van Gieson stains were negative in the epidermis and in the crater. The overall histological appearance in these 13 cases was consistent with reactive perforating collagenosis.
3. In the last case, numerous altered basophilic elastic fibres encrusted with calcium salts seen in the reticular dermis. Von kossa stain was used to stain the calcium. Channels extruding inflammatory and elastotic debris from the reticular dermis to the overlying epidermis was also seen. Verhoeff van Gieson stain was used to stain the elastic fibres. The overall

histological appearance in this case was consistent with perforating calcific elastosis.

ASSOCIATED DISEASES

Table 11: Associated diseases

Types of perforating dermatoses	DM	CRF	HYPOTHR	HT
Kyrle's disease	12	11	1	-
Reactive perforating collagenosis	4	-	-	-
Perforating calcific elastosis	-	-	-	1
Total	16	11	1	1

DM – Diabetes mellitus

CRF – Chronic renal failure

HYPOTHR - Hypothyroidism

HT – Hypertension

Twenty (67%) patients had at least one systemic disease. The commonest association was diabetes mellitus followed by chronic renal failure, hypothyroidism and hypertension.

Of the 16 patients with diabetes mellitus, 2 (12.5%) had insulin dependent diabetes mellitus (IDDM), and 14(87.5%) had non-insulin dependent diabetes mellitus (NIDDM).

Five of eleven chronic renal failure patients (45%) were on hemodialysis treatment.

In 9 of 11 patients (82%) with chronic renal failure, the cause of kidney disease was diabetes mellitus, and in 2 (18%) glomerulonephritis.

DISCUSSION

The study was conducted during the period June 2008 to June 2010 at the Department of Dermatology, Government Rajaji Hospital, Madurai Medical College, Madurai.

Incidence

30 cases of perforating dermatoses were diagnosed in about 1,15,368 patients who attended the skin OPD during the period of study.

In our study, kyrle's disease was the commonest type (54%) followed by reactive perforating collagenosis (43%) and perforating calcific elastosis (3%). Acquired type (70%) was more common compared to inherited form (30%).

In our study, only reactive perforating collagenosis was seen in the inherited form. Kyrle's disease was not seen. Joseph et al[101], in his study, reported that kyrle's disease is always associated with a systemic disorder and seen only in acquired perforating dermatoses. But its occurrence in a familial setting is also reported by Viswanathan S et al[21] and Aram et al[36] in their studies.

Age distribution

The age of onset of lesions in the majority of acquired perforating dermatoses patients (62%) were between 41 – 60 years which is similar to study by Saray et al[88.]

In our study, majority of patients of kyrle's disease fall in the age group from 41-60 years whereas Joseph et al in his study observed 31-50 years as common age group. The majority of familial reactive perforating collagenosis patients (78%) had the onset of lesions between 11 – 20 years of age as against 0 - 10 years reported by Bhat YJ et al.[23]

According to our study, in the inherited group, 67% of the patients were between 21 – 40 years of age, when they presented to us. Even though the onset was earlier, they presented to us at a later period only. This may be due to the asymptomatic nature of the disease.

Sex distribution

Preponderance of males was noted in our study which is in concordance with the study by Saray et al. On analyzing the incidence in the literature, it is varied in different studies. The sex distribution is equal for acquired perforating dermatoses and reactive perforating collagenosis.[11,23] In kyrle's disease, a female preponderance has been noted in some series[22] whereas Joseph et al has recorded a equal sex distribution.

Family history

In our study, family history of perforating dermatoses was present in all the 9 patients of inherited type. There was no family history in any of the patients with acquired perforating dermatoses.

Seasonal variation

Cold exacerbation was seen in 5 patients (56%) of familial reactive perforating collagenosis. This is in concordance with the study by Bhat YJ et al, who recorded 60% in their patients. But recurrences in summer has also been noted in the study by Ramesh V et al.[24]

Trauma and cold induces the degeneration of collagen with thinning of epidermis in genetically predisposed individuals.

Duration

The mean duration of disease was 7 months for acquired perforating dermatoses which is similar to study by Saray et al.

Morphology

The lesions of perforating dermatoses had varied morphologies resembling kyrle's disease (hyperkeratotic papules) in 54%, reactive perforating collagenosis (umbilicated papules with central keratotic plug) in 43% and

perforating calcific elastosis (erythematous papules arranged in the periphery of a central atrophic plaque in annular and serpiginous pattern) in 3%.

Distribution

Lower extremities are the most commonly involved site in acquired perforating dermatoses as stated by Saray et al who reported a frequency of 73 percent. This was the case in our study, with extensor surfaces of the lower extremities involvement in 17 patients (81%), upper extremities in 12 patients (57%), trunk in 11 patients (52%) and head in 3 patients (14%) of acquired perforating dermatoses. Multisite involvement was noted in 15 patients (71%). However unusual presentation on the face and scalp were also observed.

In perforating calcific elastosis, Hicks et al[13] and Kazakis et al[102] suggested that the traumatic effect of repeated pregnancies on elastic tissue explain the localization of skin lesion to the periumbilical area as observed in our patient.

Symptoms

Itching was the main complaint in 63% of our patients, which was most commonly encountered with acquired perforating dermatoses than with inherited form. Only one patient with familial reactive perforating collagenosis had pruritus. This patient with early onset (14 years of age) of skin lesions presented to us at the age of 60 years with large intensely pruritic lesions which

healed with scarring, indicating that the lesions become more profuse and enlarged with age unless treatment is given. Similar observations were also made by Kachhawa D et al[103] and Bhat YJ et al in their studies.

Two patients (7%) had pain, which is an unexpected symptom for acquired perforating dermatoses. Saray et al reported pain in 9 percent of patients in his study.

Koebner phenomenon

Koebnerization, which is frequently reported in perforating dermatoses, was observed in 53 percent of our patients.

Among the patients with acquired perforating dermatoses, koebner's phenomenon was present in 57% as against 32% reported by Saray et al. Frequent association of acquired perforating dermatoses lesion with pruritus, localization of the lesion mostly on the trauma prone areas, and presence of the koebner phenomenon in most of our cases suggest that mild superficial trauma (ex. scratching due to pruritus) may in fact be an important aetiological factor in the aetiopathogenesis of acquired perforating dermatoses.

Histopathology

As previously stated in the literature, we observed histopathological features consistent with each of the perforating dermatoses.

Kyrle like histopathological features were the most common (54%), followed by reactive perforating collagenosis (43%) which is in concordance with the study done by Saray et al. Perforating calcific elastosis like histopathological feature was noted in one patient.

Patterson JW[63] documented the lesions with histological features of perforating folliculitis, reactive perforating collagenosis and kyrle's disease in the same patient with acquired perforating dermatoses. Moreover, Rapini and coworkers[10] reported combined transepidermal elimination of both collagen and elastin in their four patients with acquired perforating dermatoses.

They proposed that varying histological findings in this disease may represent the different stages or different types of lesions in the same pathological process. However, we did not observe such overlapping features in our patient group. Saray et al in their study also recorded the similar findings like our study.

Moreover, it is also possible that we have been unable to observe the different stages of the histopathological evaluation because of the fact that we have taken only one biopsy from each patient. However, on the basis of distinctive histopathological findings with the absence of overlapping histopathological features in our study, we think that acquired perforating dermatoses consists of four different types of perforating disorders, namely,

kyrle's disease, reactive perforating collagenosis, perforting folliculitis and elastosis perforans serpiginosa like perforating disorders.

Patterson JW, in his study noted both collagen and elastin in the early, non umbilicated lesions, whereas collagen was observed in the umbilicated ones. Fibrous component was the only material eliminated in late lesions, probably due to the degeneration of both collagen and elastin.

In contrast to these early findings, we observed neither collagen nor elastin elimination in most of the non umbilicated lesions. However, collagen elimination was observed in the umbilicated ones, which was similar to the findings in the above mentioned study.

Associations

In our study, majority (67%) of our patients had at least one systemic disease, and diabetes mellitus (76%) and chronic renal failure (52%) were the most common diseases associated with acquired perforating dermatoses.

Two of our patients had insulin dependent diabetes mellitus (IDDM), and most (14) had non insulin dependent diabetes mellitus (NIDDM) similar to study by Saray et al. Other investigators[4,104] have also found that NIDDM is more frequent in patients with acquired perforating dermatoses. In contrast, Morton and coworkers[15] observed that acquired perforating dermatoses is more often associated with IDDM compared with NIDDM.

In diabetes mellitus, the proposed mechanism is that, trauma from scratching may cause dermal necrosis due to poor blood supply that results from vasculopathy, with necrotic material then being extruded through the epidermis.[88]

Chronic renal failure was the second most frequent (52%) disease associated with acquired perforating dermatoses in the present study. In 9 of eleven patients (82%) with chronic renal failure, the cause of kidney disease was diabetes mellitus, and in 2 (18%) glomerulonephritis, findings similar to studies done by Saray et al and Joseph et al were seen.

In the literature, epidermal or dermal abnormalities such as alterations in collagen or elastic fibres due to metabolic disturbances related to chronic renal failure have been suggested as underlying factors in acquired perforating dermatoses patients with chronic renal failure.[88]

In patients with chronic renal failure, acquired perforating dermatoses often occurs following dialysis.[15,104] However, the lesions may also start in the pretreatment period.[15,60] In our study, acquired perforating dermatoses developed after the initiation of dialysis treatment in five patients with chronic renal failure.

Hypothyroidism was associated in one patient with acquired perforating dermatoses. Association of acquired perforating dermatoses with hypothyroidism has been described in earlier studies by Faver IR et al.[4]

Hypertension was seen in one patient with periumbilical perforating calcific elastosis, who was an obese, multiparous woman with no characteristic lesions and family history of pseudoxanthoma elasticum.

There was no systemic association seen in any of our patients with familial reactive perforating collagenosis as described in earlier studies by Bhat YJ et al.

Interesting observation

An unusual finding of this study was that Kyrle's disease was detected in one patient in whom neither a systemic disease nor any other dermatological problem was observed. There are only few reports of acquired perforating dermatoses occuring in otherwise healthy people.[96,105] Kalla G et al[106] and Saray et al have reported similar cases in their studies.

SUMMARY

Thirty patients, diagnosed with perforating dermatoses, based on history, clinical features and histopathology were included in the study.

Incidence

The incidence was 1.3 per 10,000 among 1,15,368 new patients who attended the skin OPD during the period of study.

Kyrle's disease was the commonest type (54%), followed by reactive perforating collagenosis (43%) and perforating calcific elastosis (3%).

Age

78% of the patients in the inherited form had the onset of lesions between 11 – 20 years.

62% of the acquired perforating dermatoses patients had the onset of lesions between 41 – 60 years.

Sex

Preponderance of males was noted in our study.

Family history

Family history of perforating dermatoses was present in all the 9 cases in the inherited group.

Seasonal variation

Winter exacerbation was seen in 56% of familial reactive perforating collagenosis patients.

Morphology and distribution

Hyperkeratotic papules were present in 53%, umbilicated papules with keratotic plugging in 43% and annular atrophic plaque with erythematous papules in the periphery in 3% of the patients.

Lower extremities (73%) were the most commonly involved site, followed by the upper extremities (63%), trunk (57%) and head (23%). Multisite involvement was also common (71%).

Symptoms

Pruritus was present in 63% and pain in 7% of our patients. 30% were asymptomatic.

Koebner phenomenon

Koebner phenomenon was seen in 53% of our patients.

Histopathology

Histopathological features consistent with kyrle's disease were seen in 16 patients, reactive perforating collagenosis in 13 patients and perforating calcific elastosis in one patient.

Associations

In this study, diabetes mellitus was the commonest associated disease, followed by chronic renal failure, hypothyroidism and hypertension.

Non insulin dependent diabetes mellitus (NIDDM) was more commonly seen than insulin dependent diabetes mellitus (IDDM).

The commonest cause of kidney disease in chronic renal failure patients was diabetes mellitus (82%), followed by glomerulonephritis (18%).

Interesting presentation of one case of acquired perforating dermatoses with no systemic association was seen.

CONCLUSION

1. Perforating dermatoses is a rare skin disease comprising only a very small percentage of patients (1.3 per 10,000) attending the skin OPD.
2. Kyrle's disease is the most common perforating dermatoses, followed by reactive perforating collagenosis.
3. The age of onset of skin lesions for majority of the patients in the inherited form is 11 – 20 years and in acquired, 41 – 60 years.
4. Preponderance of males is noted.
5. Lower extremities are the most frequent site of involvement.
6. Clinicopathological examination is important in arriving at the diagnosis.
7. Non insulin dependent diabetes mellitus is the most frequent association seen with acquired perforating dermatoses.
8. In chronic renal failure patients with acquired perforating dermatoses, the contributing factors are either diabetes mellitus or hemodialysis.
9. An interesting case of acquired perforating dermatoses with no systemic association is also noted.

KEY TO MASTER CHART

P = Present

F.H = Family History

COLD = Cold exacerbation

MORP = Morphology

1 = Keratotic plugged, umbilicated papules

2 = Keratotic plugged, umbilicated papules and plaques

3 = Hyperkeratotic papules

4 = Erythematous papules arranged in the periphery of a central atrophic plaque in annular and serpiginous pattern

DISTRIB = Distribution

H = Head

T = Trunk

UL = Upper limb

LL = Lower limb

KOEB = Koebner phenomenon

DM = Diabetes mellitus

CRF = Chronic renal failure

GN = Glomerulonephritis

HD = Hemodialysis

THY = Hypothyroidism

IDDM = Insulin dependent diabetes mellitus

NIDDM = Non insulin dependent diabetes mellitus

DUR = Duration

HP-E.M = Histopathology – Eliminated material

KD = Kyrle’s disease

RPC-I = Reactive perforating collagenosis – Inherited

RPC-A = Reactive perforating collagenosis – Acquired

PCE = Perforating calcific elastosis

Yrs = years

Mo = months

MASTER CHART

S.NO	NAME	AGE/ SEX	F.H	AGE OF ONSET	DURATION	SYMPTOMS	COLD	MORP	SCAR	DISTRIB	KOEB	ASSOCIATIONS			HP-E.M	DIAGNOSIS
												DM/DUR	CRF/DUR	OTHERS		
1	Shanthi	27/F	P	12 years	10 years	_	P	1	P	UL,LL,H	_	_	_	_	Collagen	RPC-I
2	Chandran	56/M	P	10 years	46 years	_	_	2	P	LL,UL	_	_	_	_	Collagen	RPC-I
3	Sophi	49/F	–	49 years	4 months	Pruritus	_	3	_	UL,LL	P	NIDDM/4 yrs	P/7 mo	_	_	KD
4	Meenakshi	63/F	_	63 years	1 month	Pruritus	_	1	_	LL	P	NIDDM/10 yrs	_	_	Collagen	RPC-A
5	Yasar Arafat	16/F	P	14 years	2 years	_	_	1	_	UL,T	_	_	_	_	Collagen	RPC-I
6	Alamelu	39/F	_	39 years	6 months	Pruritus	_	3	_	LL	P	_	P/16 yrs	HD/6 yrs	_	KD
7	Ramar	35/M	P	10 years	25 years	_	_	1	P	T,UL,LL	P	_	_	_	Collagen	RPC-I
8	Krishnaveni	49/F	_	49 years	1 month	Pruritus	_	3	_	LL,UL	P	_	P/3 yrs	GN/5 yrs	_	KD
9	Sudharsan	57/M	_	57 years	3 months	Pruritus	_	1	_	LL	P	NIDDM/8 yrs	_	_	Collagen	RPC-A
10	Fathima	40/F	_	38 years	2 years	Pruritus	_	1	_	UL,LL	_	NIDDM/6 yrs	_	_	Collagen	RPC-A
11	Gnanam	44/M	_	44 years	1 month	Pruritus	_	3	_	T,UL,LL	P	IDDM/2 yrs	_	_	_	KD
12	Vellai	60/M	_	60 years	1 month	Pruritus	_	3	_	UL,LL,T	P	NIDDM/15 yrs	_	_	_	KD
13	Samsudeen	40/M	_	38 years	2 years	Pruritus	_	3	P	UL,T,LL	_	_	_	_	_	KD
14	David	28/M	P	17 years	11 years		_	1	_	UL	_	_	_	_	Collagen	RPC-I
15	Saroja	52/F	_	52 years	1 month	Pain	_	3	_	UL,T,H	_	NIDDM/2 yrs	P/1 year	HD/6 mo	_	KD

COLOUR PLATES

KYRLE'S DISEASE

Hyperkeratotic papules over thigh and back

Hyperkeratotic papules over gluteal region and knee joint

KYRLE'S DISEASE

Koebner phenomenon over elbow and knee joint

PERFORATING PERIUMBILICAL CALCIFIC ELASTOSIS

REACTIVE PERFORATING COLLAGENOSIS

Umbilicated papules and plaques over leg and forearm

Umbilicated papules and plaques over scalp

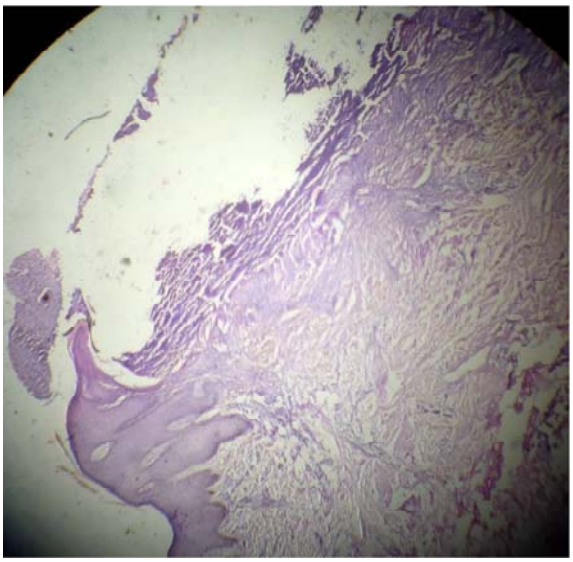
REACTIVE PERFORATING COLLAGENOSIS

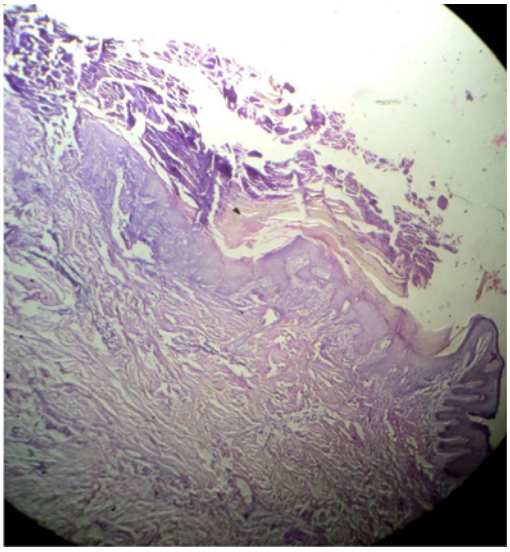
Umbilicated papules -arm, back

Koebner phenomenon - plaque over leg

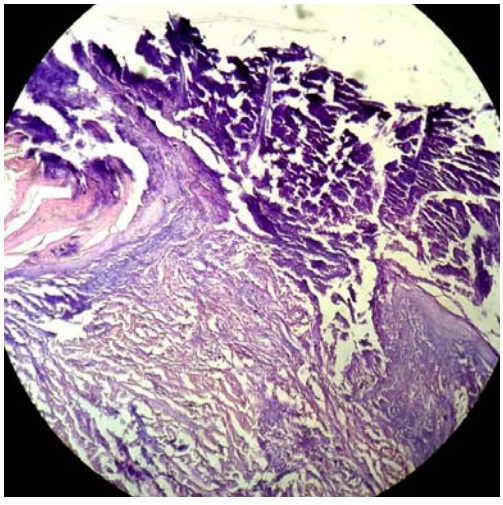
Varioliform scarring over back and face

REACTIVE PERFORATING COLLAGENOSIS

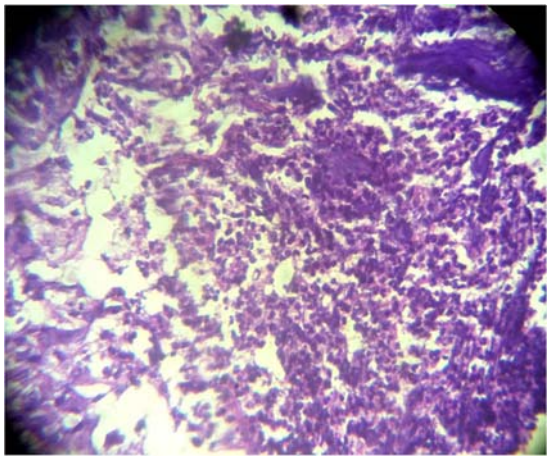




Cup shaped invagination of epidermis filled with plug containing keratin and cellular debris

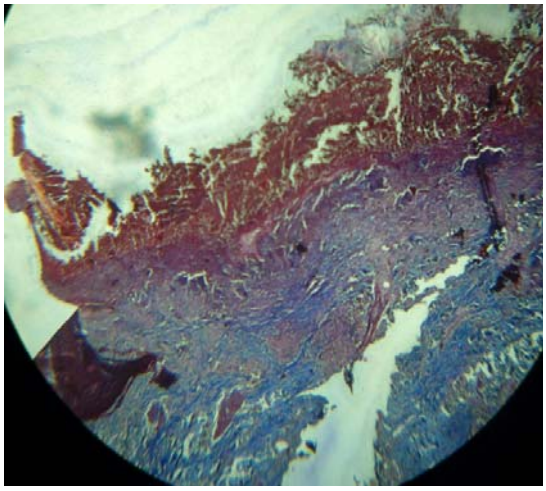


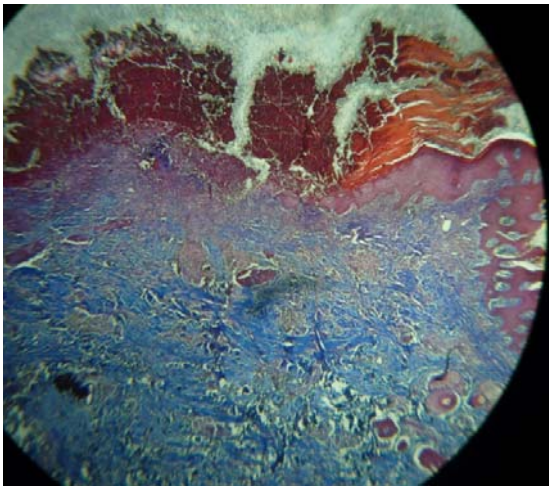
Transepidermal elimination of collagen



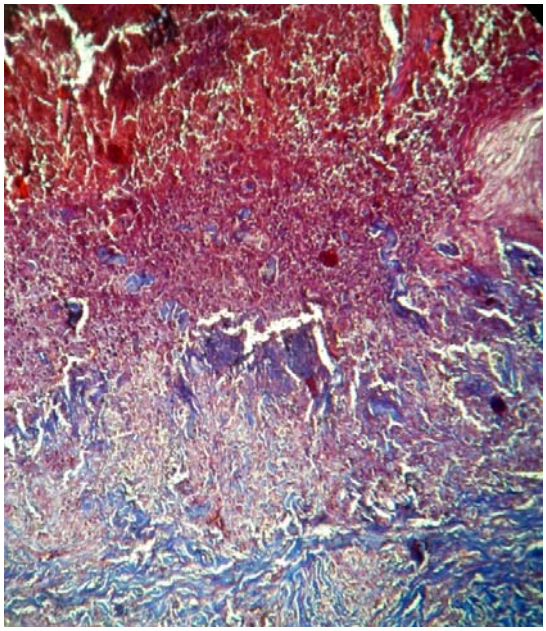
Inflammatory infiltrate

REACTIVE PERFORATING COLLAGENOSIS



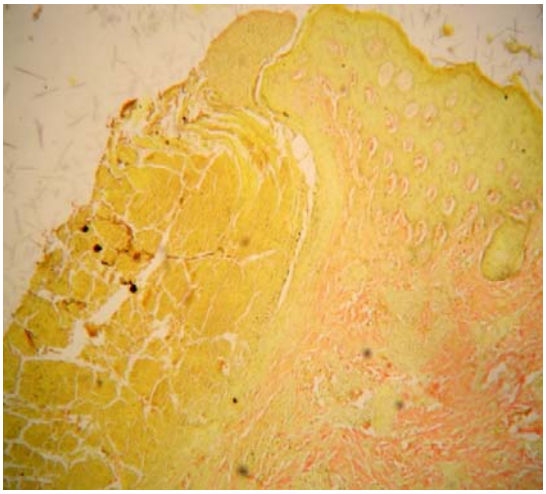


Masson trichrome stain for collagen



MT stain -Transepidermal elimination of collagen

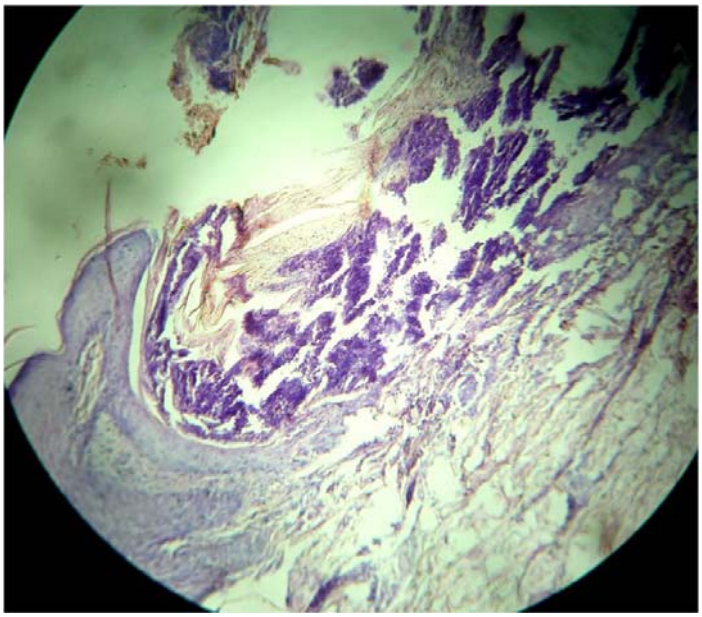
collagen stained blue

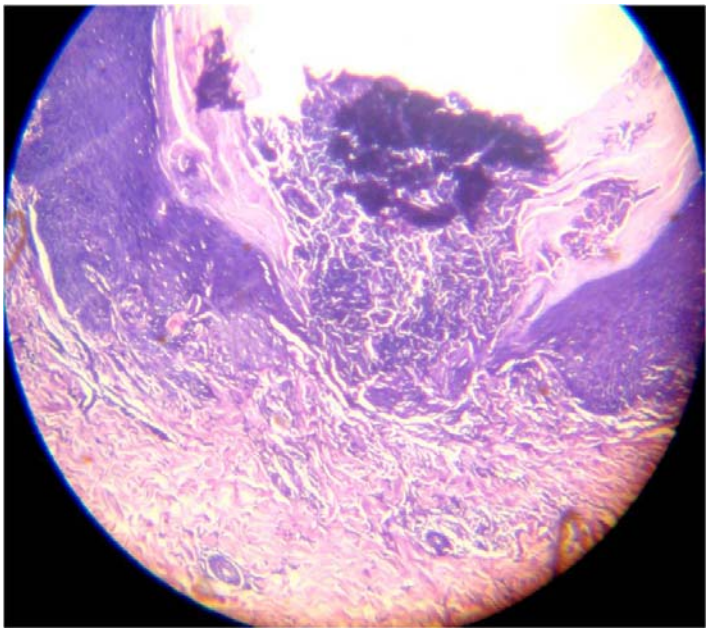


Verhoeff van Gieson stain

collagen stained red

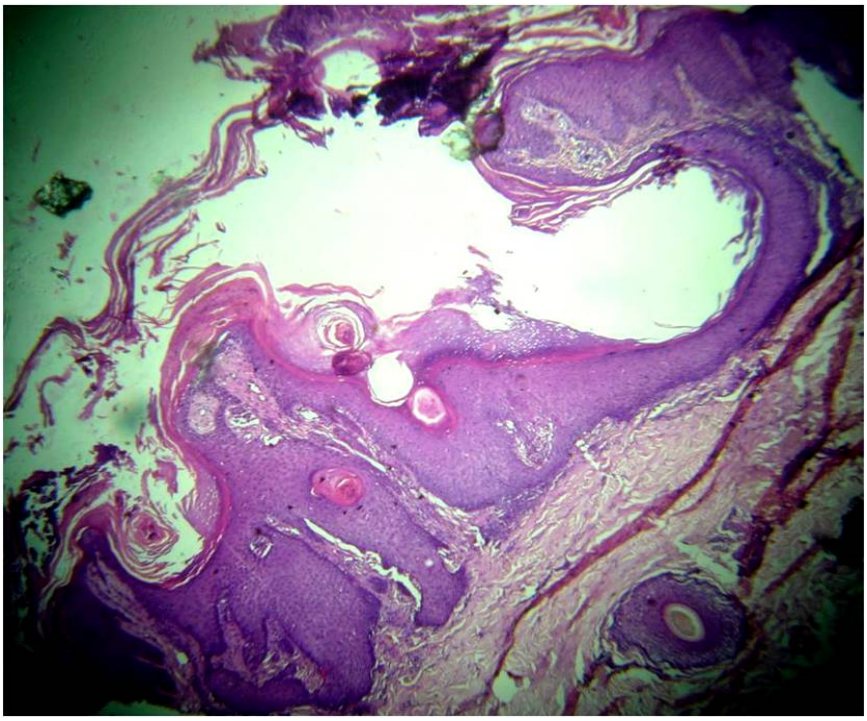
REACTIVE PERFORATING COLLAGENOSIS

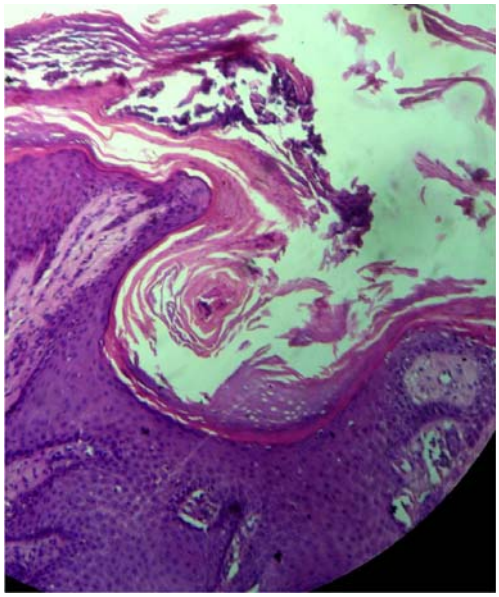


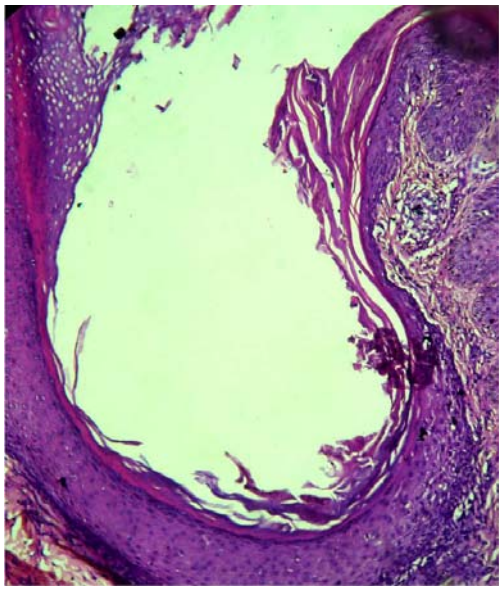


Transepidermal elimination of collagen fibres

KYRLE'S DISEASE

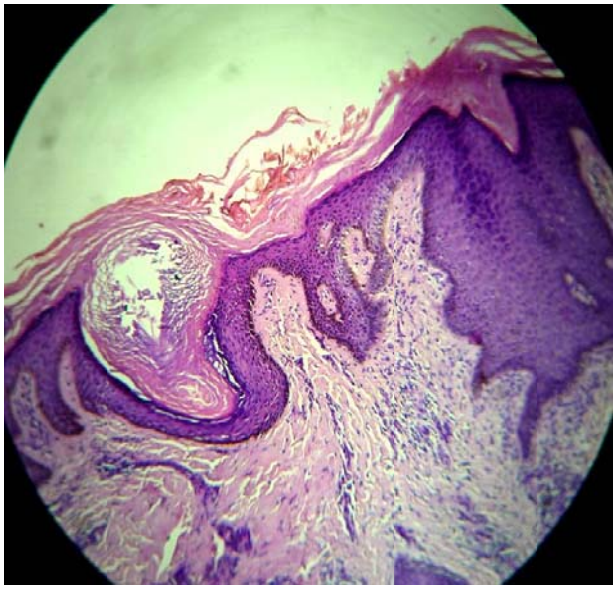




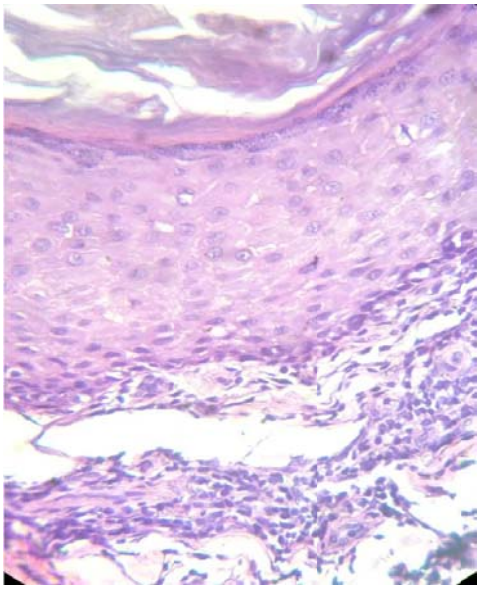


Epidermal invagination filled with keratotic plug admixed with cellular debris

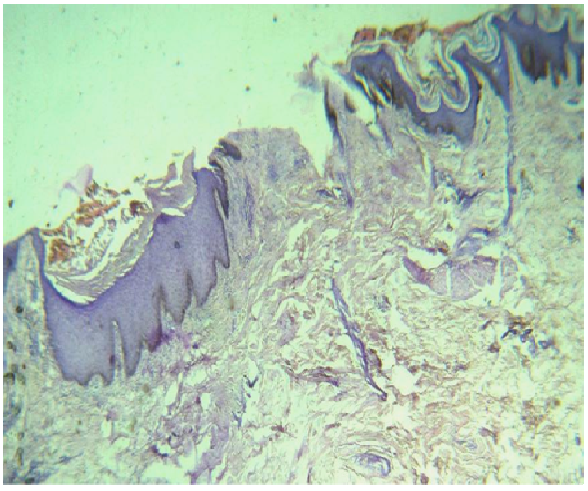
KYRLE'S DISEASE

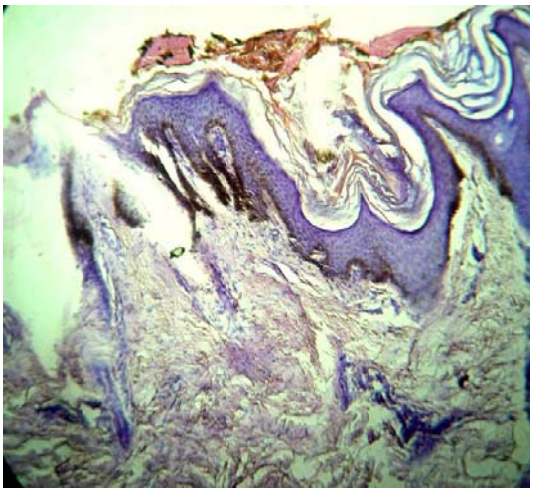


Keratotic plugging

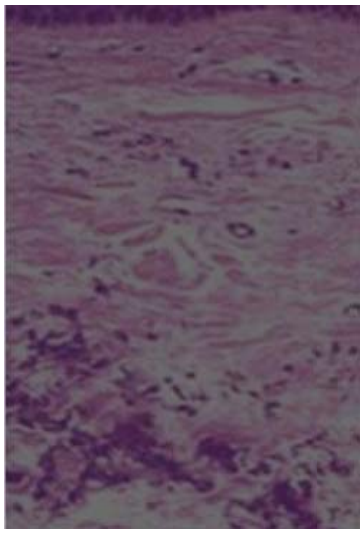


Inflammatory infiltrate

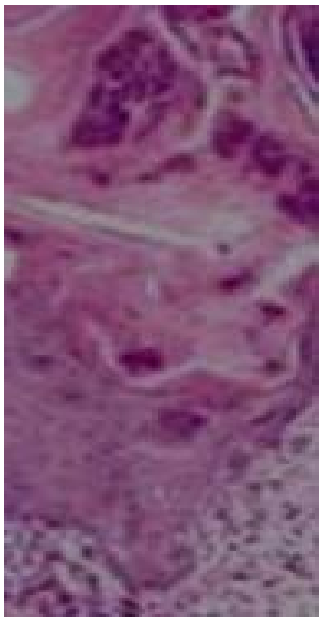




PERFORATING CALCIFIC ELASTOSIS



Irregular calcified elastic fibres in the reticular dermis



Epidermal hyperplasia with keratotic plug admixed with cellular debris and calcified elastic fibres

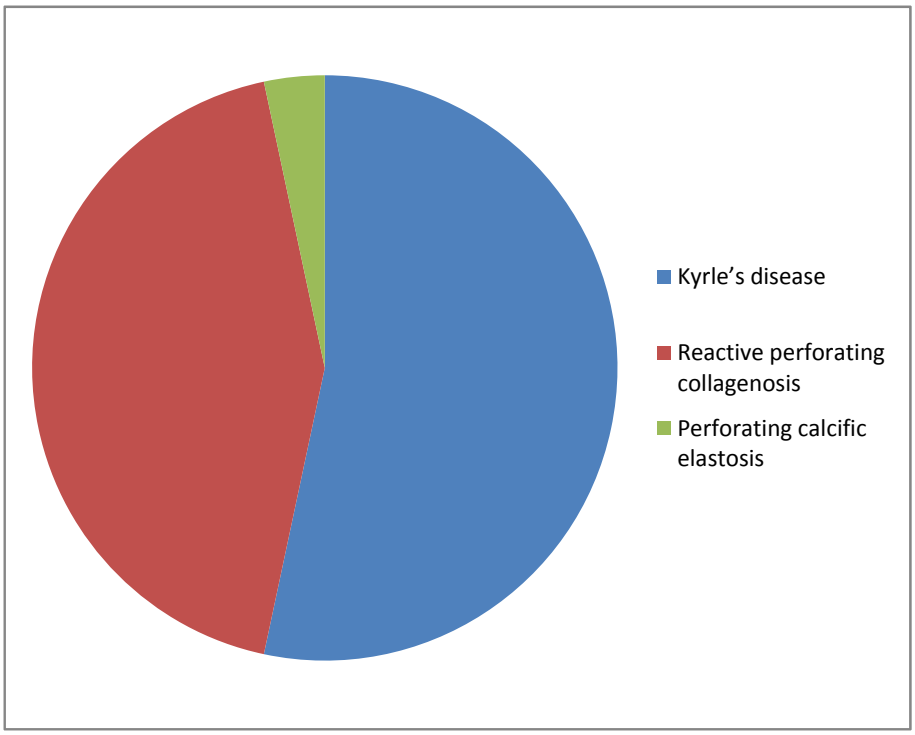


Figure 1: Clinical Types

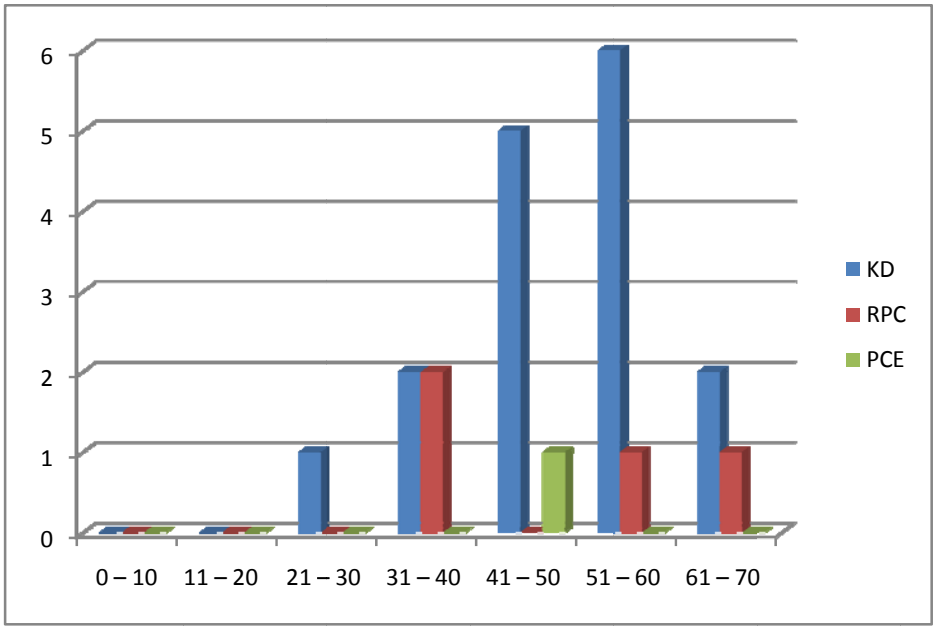


Figure 2: Age Distribution

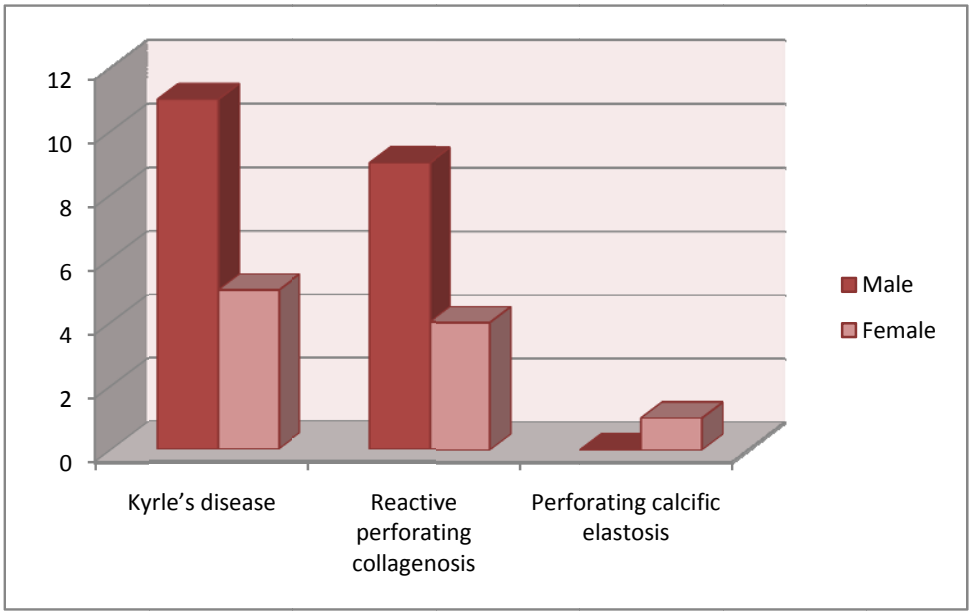


Figure 3: Sex Distribution

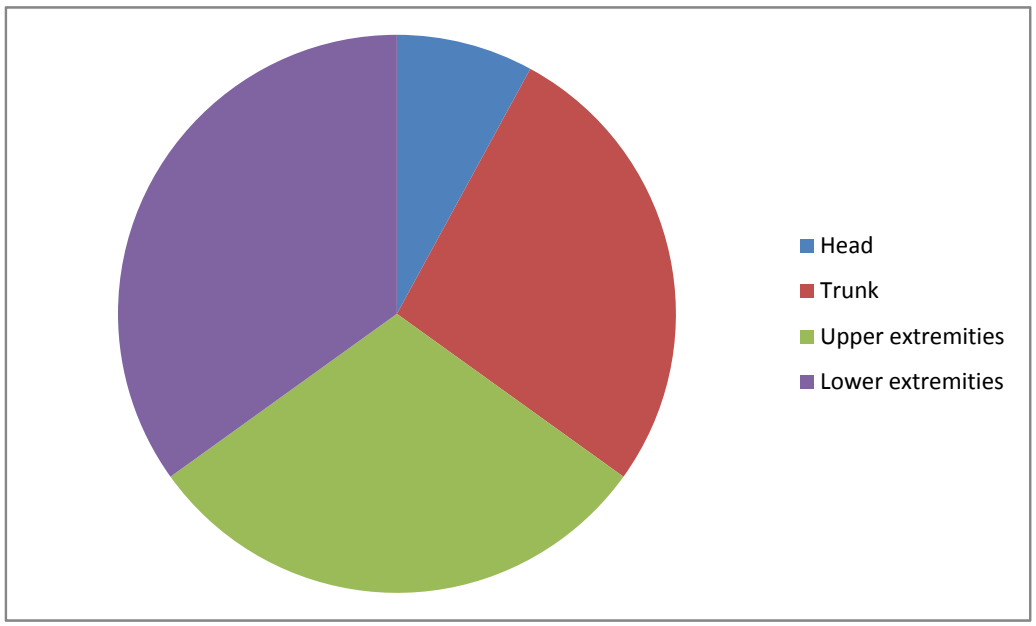


Figure 4: Regional Distribution

PROFORMA

Case no:

Name:

Age:

Sex:

Hosp no:

Occupation:

Income:

Socioeconomic status:

Address:

History of skin lesion:

- Age of onset
- Duration
- Site of first lesion
- Evolution of lesion
- Healing spontaneously or with treatment
- Healing with hypo/hyperpigmentation/scarring

History of pruritus

History of lesions following trauma

History of any drug intake for other ailments

History of any seasonal variation

General history

- H/o diabetes – age of onset, duration, treatment +/-
- H/o renal disease – age of onset, duration, treatment+/- , dialysis +/-
- H/o liver disorder
- H/o endocrine diseases
- H/o infection
- H/o malignancy

Family history

Personal history

- Smoking/alcohol
- Marital status

GENERAL EXAMINATION

- General condition – built, nutrition
- Anemia +/-
- Jaundice+/-
- Cyanosis+/-
- Clubbing +/-
- Pedal edema+/-
- Lymphadenopathy+/-
- Body weight
- Pulse
- Blood pressure

Cardiovascular system

Respiratory system

Abdomen

Others

DERMATOLOGICAL EXAMINATION:

Active skin lesion

- Number, site:
- Morphology:
- Distribution: groups/discrete

along lines of trauma

Healing lesion

Hypo/hyperpigmentation

Scarring

Palms & soles

Mucosal lesions

Hair & nail

Any other skin lesions

INVESTIGATIONS:

- Complete hemogram
- Renal function tests
- Liver function tests
- Blood sugar
- Urine examination
- Serum calcium
- Thyroid profile
- Serology – HIV,HBV,HCV

- Skin biopsy

  Site:

  Findings:

  Special Stain:

FINAL DIAGNOSIS:

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